

# A haemodynamic conundrum: a case report of a patient with concurrent pulmonary arterial hypertension and hypertrophic obstructive cardiomyopathy

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## Background

The co-existence of hypertrophic obstructive cardiomyopathy (HOCM) and pulmonary arterial hypertension (PAH) is extremely rare and poses a management conundrum. This is the first case report in the published literature to describe the diagnosis and management of a patient with both conditions.

## Case summary

A 49-year-old female with a history of HOCM and recently diagnosed scleroderma presented to the clinic with progressive dyspnoea. Transthoracic echocardiogram demonstrated left ventricular outflow tract (LVOT) obstruction at rest, and elevated pulmonary artery (PA) pressure. Cardiac catheterization (CC) demonstrated an LVOT gradient of 150 mmHg, PA pressure of 88/32 mmHg, pulmonary capillary wedge pressure (PCWP) 12 mmHg, pulmonary vascular resistance 14.8 Wu, and a cardiac index of 1.6 L/min/m<sup>2</sup>. The differential diagnosis for the dyspnoea included combined pre- and post-capillary pulmonary hypertension from longstanding HOCM vs. scleroderma associated PAH. Tadalafil was added to the patient's medical regimen of metoprolol but it was stopped because the patient developed pulmonary oedema. Alcohol septal ablation was undertaken with improvement in the LVOT gradient, but only a modest improvement in her dyspnoea. Repeat CC demonstrated worsening PAH. Vasodilatory testing with nitric oxide led to an improvement in the PA pressure with minimal increase of the PCWP. Hence, she was started on treprostinil and macitentan, with significant improvement in her dyspnoea on follow-up.

## Conclusion

In patients with concurrent HOCM and advanced PAH, a multidisciplinary treatment approach is needed to rapidly and safely optimize the background of HOCM in order to permit the use of PAH-specific medications.

## Keywords

Hypertrophic cardiomyopathy • Pulmonary hypertension • Haemodynamics • Alcohol septal ablation

## Learning points

- Understand the haemodynamic interaction between World Health Organization group 1 pulmonary hypertension (PH) and hypertrophic obstructive cardiomyopathy (HOCM).
- Understand the challenges in the management of patients with concomitant PH and HOCM.

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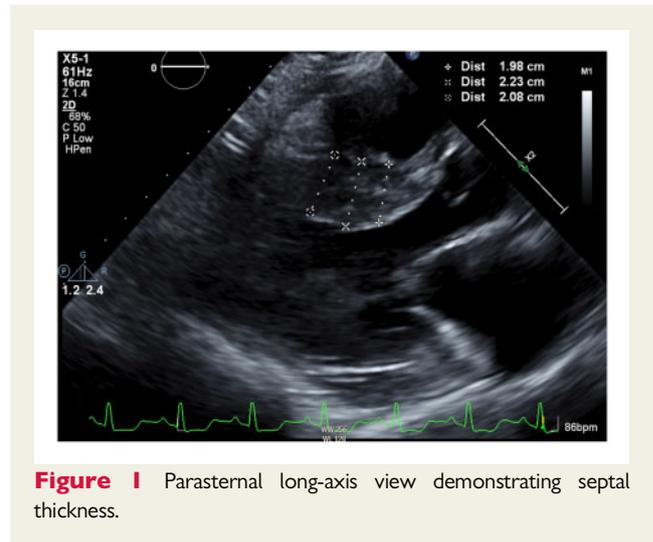
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## Introduction

The co-existence of hypertrophic obstructive cardiomyopathy (HOCM) and pulmonary arterial hypertension (PAH) represents a management dilemma that requires an in-depth understanding of cardiac and pulmonary haemodynamics and physiology. In this case report, we describe a patient with both conditions and discuss the management challenges and treatment options.

## Timeline

2015	<ul style="list-style-type: none"> <li>• Diagnosis of hypertrophic obstructive cardiomyopathy. Patient started on metoprolol succinate.</li> </ul>
May 2019	<ul style="list-style-type: none"> <li>• Evaluation of possible scleroderma.</li> </ul>
August 2019	<ul style="list-style-type: none"> <li>• Progressive New York Heart Association (NYHA) class III dyspnoea over the past 6 months.</li> <li>• Referral to our institution for evaluation of dyspnoea.</li> <li>• New diagnosis of Scleroderma.</li> </ul>
September 2019	<ul style="list-style-type: none"> <li>• Transthoracic echocardiogram (TTE): left ventricular outflow tract (LVOT) obstruction at rest, and elevated pulmonary artery (PA) systolic pressure.</li> <li>• Cardiac catheterization (CC): mean PA 88/32 (52), pulmonary capillary wedge pressure (PCWP) 12, transpulmonary gradient 40, pulmonary vascular resistance 14.81, cardiac index of 1.6 L/min/m<sup>2</sup>.</li> <li>• Pulmonary function tests and computed tomography chest: unremarkable, no pulmonary embolism.</li> </ul>
November 2019	<ul style="list-style-type: none"> <li>• Initiation of tadalafil lead to worsening of dyspnoea.</li> <li>• Alcohol septal ablation undertaken.</li> </ul>
February 2020	<ul style="list-style-type: none"> <li>• Symptoms unchanged.</li> <li>• TTE: improvement in the resting LVOT gradient.</li> </ul>
May 2020	<ul style="list-style-type: none"> <li>• Persistent dyspnoea NYHA III.</li> <li>• Implantable cardioverter-defibrillator settings changed to chronically pace the right ventricle which led to abolition of the resting LVOT gradient, and further reduction of the provokable gradient.</li> </ul>
October 2020	<ul style="list-style-type: none"> <li>• Modest improvement in her dyspnoea.</li> <li>• Repeat CC demonstrated worsening pulmonary arterial hypertension. Vasodilatory testing with nitric oxide: non-responder. However, some improvement in the PA pressure noted with minimal increase of the PCWP.</li> <li>• Patient started on treprostinil and macitentan.</li> </ul>
March 2021	<ul style="list-style-type: none"> <li>• Significant improvement in her dyspnoea at 6-month follow-up.</li> <li>• Follow-up TTE demonstrated improved PA systolic pressure and right ventricular function.</li> </ul>



**Figure 1** Parasternal long-axis view demonstrating septal thickness.

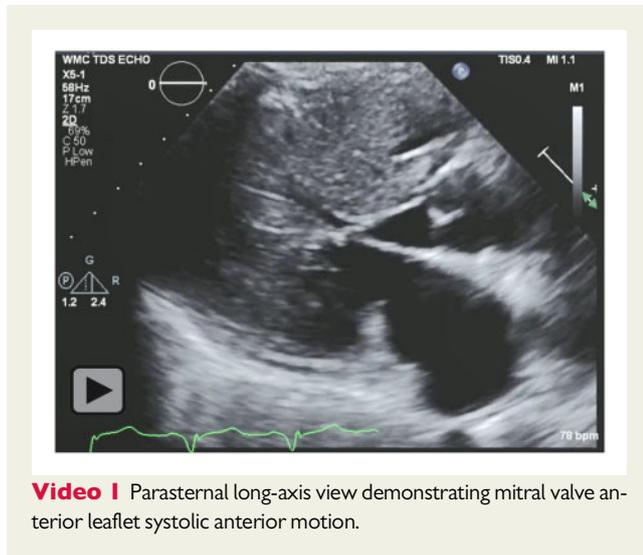
## Case presentation

A 49-year-old Caucasian female with a history of HOCM was evaluated in the office for worsening New York Heart Association class III dyspnoea over the past 6 months. Initial history and examination were remarkable for prior Raynaud's phenomenon, a crescendo systolic murmur that increased with the Valsalva manoeuvre and hand telangiectasias without sclerodactyly. The patient had been diagnosed with obstructive HOCM 6 years earlier and was treated with metoprolol succinate 100 mg daily and an implantable cardioverter-defibrillator (ICD) for primary prevention. She was recently referred to a rheumatologist for evaluation of possible scleroderma.

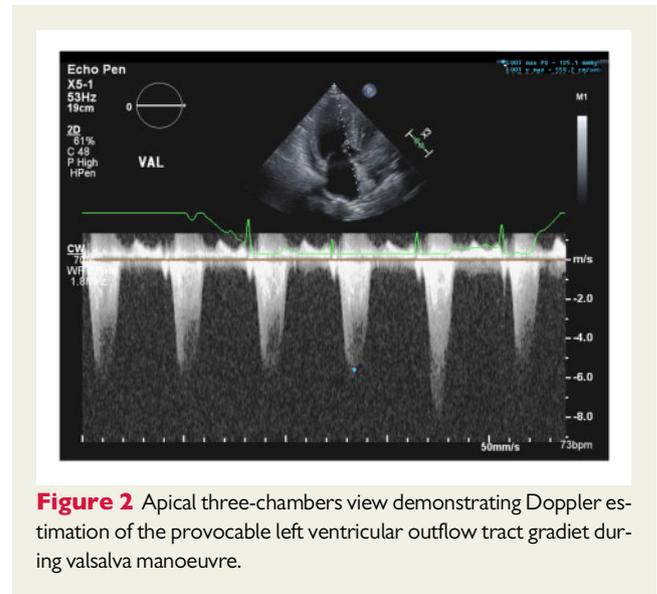
Transthoracic echocardiogram (TTE) demonstrated asymmetrical left ventricular hypertrophy (LVH) with a maximal septal thickness of 2.2 cm (Figure 1), systolic anterior motion (SAM) of the mitral valve (Video 1), and a dynamic left ventricular outflow tract (LVOT) gradient of 56 mmHg at rest and 125 mmHg with Valsalva (Figure 2). Right ventricular (RV) function was mildly reduced, and the pulmonary artery (PA) systolic pressure was estimated at 75 mmHg. Subsequently, left and right cardiac catheterization (RHC) revealed normal coronary arteries, provokable LVOT gradient of 150 mmHg, PA pressure of 88/32 (52) mmHg, pulmonary capillary wedge pressure (PCWP) 12 mmHg, transpulmonary gradient (TPG) 40, pulmonary vascular resistance (PVR) 14.8 Woods units (Wu), and a cardiac index (CI) of 1.6 L/min/m<sup>2</sup>. Anti-centromere antibodies were positive. Computed tomography of the lungs, pulmonary function tests, and a ventilation-perfusion scan were unremarkable.

The differential diagnosis included combined pre- and post-capillary pulmonary hypertension (PH) from her longstanding HOCM, with the scleroderma features being incidental. Alternatively, limited scleroderma involving the pulmonary vasculature and contributing to her PH was considered.

The patient was started on tadalafil but this was stopped because of increased dyspnoea and gastric reflux symptoms. Surgical myectomy was considered but given the increased risk in the presence of severe PH, the decision was made to proceed with alcohol septal ablation (ASA). Over the months following the ASA, the patient had a



**Video 1** Parasternal long-axis view demonstrating mitral valve anterior leaflet systolic anterior motion.



**Figure 2** Apical three-chambers view demonstrating Doppler estimation of the provokable left ventricular outflow tract gradient during valsalva manoeuvre.

modest initial improvement in her symptoms, but then the dyspnoea worsened. Transthoracic echocardiogram performed 6 months after ASA showed significant improvement of the provokable and resting gradients across the LVOT. To further optimize her prior to starting PAH-specific medications, her ICD was reprogrammed to pace the RV apex to induce left ventricular (LV) dyssynchrony, which led to abolition of the resting LVOT gradient, and further reduction of the provokable gradient to 32 mmHg.

Given the resolution of gradients, it was felt that her dyspnoea was due to progression of scleroderma-associated World Health Organization (WHO) 1 PAH. Repeated RHC showed a PA pressure mean 61 mmHg, PVR 34.1 Wu, and CI 1 L/min/m<sup>2</sup> in the setting of a PCWP of 4 mmHg. Vasodilatory testing with nitric oxide (NO) showed improvement in the PA mean pressure 56 mmHg, PVR 20.9 Wu, and CI 1.4 L/min/m<sup>2</sup>, and minimal increase of the PCWP (6 mmHg). However, the improvement in the patient's haemodynamics did not meet the threshold for considering calcium channel blocker treatment (non-responder). She was subsequently started on intravenous treprostinil, a direct vasodilator acting through the prostacyclin pathway, and macitentan, an endothelin receptor antagonist. The combination therapy of treprostinil and macitentan was well tolerated by the patient. Three months after initiation of PAH-specific medication, she reports a significant improvement in dyspnoea and overall energy. Follow-up TTE demonstrated improved PA systolic pressure from 76 to 63 mmHg and improved RV function, with tricuspid annular plane systolic excursion increasing from 1.4 to 1.8 cm. Accordingly, the treprostinil dose was up-titrated from 25 to 45 ng/kg/min.

## Discussion

Hypertrophic obstructive cardiomyopathy is the most common genetic cardiac condition with a prevalence of up to 1:200 in the general population.<sup>1</sup> Up to two-thirds of HCM patients show evidence of dynamic LVOT obstruction related to SAM of the mitral valve with septal contact.<sup>2</sup> Obstructive physiology and diastolic dysfunction can

lead to progressive heart failure symptoms. In several series of HCM patients, a PA systolic pressure >35 mmHg, has been identified in 18–38% of patients, with higher prevalence seen in the obstructive HCM phenotype.<sup>3,4</sup> Interestingly, in one series, 9% of the HCM patients with PH had a PCWP ≤15 mmHg with high PVR, raising the possibility of co-existent combined pre and post-capillary PH.<sup>5</sup> PH was found to be an independent predictor of HCM morbidity<sup>3</sup> and mortality<sup>4</sup> in non-obstructive and obstructive Hypertrophic Cardiomyopathy (HCM) patients who did not undergo septal reduction therapy (SRT).

Pulmonary arterial hypertension WHO group 1 is a rare condition with a prevalence of 15–50 cases per million.<sup>6</sup> It is defined as a mean PA pressure ≥25 mmHg, a PCWP <15 mmHg, and a PVR of >3 Wu. Pulmonary arterial hypertension has complex pathophysiology characterized by an imbalance of vasoconstrictor and vasodilator peptides leading to remodelling of the pulmonary arterioles. Pulmonary arterial hypertension can be associated with connective tissue disease, especially in scleroderma patients, with a prevalence of up to 19%.<sup>7</sup> The prognosis of scleroderma associated PAH is poor with 3-year survival of approximately 60%.<sup>8</sup>

To our knowledge, this is the first case report of a patient with concurrent HOCM and WHO group 1 PAH-scleroderma, two disease states that are rising in prevalence due to heightened awareness and screening. Although PH had been reported in patients with HOCM (WHO group 2), a very high TPG and PVR should raise the possibility of another contributing process.

The haemodynamic interaction of these two pathologies poses several challenges. While several vasoactive agents are indicated in the treatment of WHO group 1 PAH, vasodilation of the pulmonary arterioles in the setting of elevated left atrial pressure due to LVOT obstruction and diastolic dysfunction from HOCM can lead to pulmonary oedema. Paradoxically, increased pre-load to the left ventricle as a result of PAH medications could potentially improve SAM and LVOT obstruction and decrease the PCWP. In this case, the use of pulmonary arterial vasodilators (tadalafil) prior to optimization of HOCM physiology lead to significant dyspnoea and early discontinuation of the medication.

HCM-related LVOT obstruction that is resistant to medical therapy can be relieved by SRT. These treatments also improve diastolic dysfunction in patients with HOCM over time.<sup>9</sup> Surgical myectomy is the preferred approach in most young patients, particularly with massive LVH and very large gradients. In this case, severe PH made induction of general anaesthesia high risk for acute haemodynamic collapse. In addition, a minimally invasive SRT, as in ASA, is more reasonable in patients with concomitant PAH and limited life expectancy.

Optimization of her HOCM physiology alone was not associated with improvement in dyspnoea, suggesting that her scleroderma-associated severe PAH was contributing to her progressive symptoms. The NO challenge administered during the RHC, 6 months after optimization of the HOCM physiology, decreased PA pressure and increased CI without increasing the PCWP. NO is a potent pulmonary arterial vasodilator that increases PA flow to the left ventricle. The lack of significant elevation of PCWP after the NO challenge reflects the success of the ASA in relieving the LVOT obstruction, and normalization of the left atrial and the diastolic LV pressures. The NO challenge helped predict that the patient is likely to tolerate PAH medications and the associated increase in the PA flow. Therefore, the ASA was pivotal in improving the LV ability to tolerate increases in preload from pulmonary vasodilator treatment. Frequent assessment of her symptoms will be necessary, as there may come a point where the improved PVR may lead to eventual elevated PCWP and shortness of breath, requiring augmented diuretics. An additional practical consideration in patients with severe PH and RV dysfunction is that they may not tolerate beta-blockers. However, in her case, some degree of negative chronotropy and contractility may be necessary for any residual LVOT gradient.

## Conclusion

This case describes the management dilemma in caring for patients that have two uncommon, yet increasingly recognized diseases. Since the prognosis of untreated PAH-scleroderma is very poor, a multidisciplinary treatment approach is needed to rapidly and safely optimize the background of HCM with obstruction in order to permit the use of PAH-specific medications.

## Lead author biography



Ahmed Hassanin, MD, MPH is a cardiovascular disease fellow at

Westchester Medical Center in New York. His hometown is Alexandria, Egypt, where he graduated from the University of Alexandria School of Medicine in 2010. His areas of interest include hypertrophic cardiomyopathy and ST-segment elevation myocardial infarction (STEMI) systems of care in resource limited communities. Dr Hassanin plans to pursue a career in interventional cardiology and global cardiovascular health.

## Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** G.M.L. is on the speakers' bureau for United Therapeutics. The other authors of this manuscript have no relationship with industry that could be perceived to bias their work.

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## References

1. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2015;**65**:1249–1254.
2. Maron MS, Hauser TH, Dubrow E, Horst TA, Kissinger KV, Udelson JE et al. Right ventricular involvement in hypertrophic cardiomyopathy. *Am J Cardiol* 2007;**100**:1293–1298.
3. Musumeci MB, Mastromarino V, Casenghi M, Tini G, Francia P, Maruotti A et al. Pulmonary hypertension and clinical correlates in hypertrophic cardiomyopathy. *Int J Cardiol* 2017;**248**:326–332.
4. Ong KC, Geske JB, Hebl VB, Nishimura RA, Schaff HV, Ackerman MJ et al. Pulmonary hypertension is associated with worse survival in hypertrophic cardiomyopathy. *Eur Heart J Cardiovasc Imaging* 2016;**17**:604–610.
5. Covella M, Rowin EJ, Hill NS, Preston IR, Milan A, Opatowsky AR et al. Mechanism of progressive heart failure and significance of pulmonary hypertension in obstructive hypertrophic cardiomyopathy. *Circ Heart Fail* 2017;**10**:e003689.
6. McGoon MD, Benza RL, Escribano-Subias P, Jiang X, Miller DP, Peacock AJ et al. Pulmonary arterial hypertension: epidemiology and registries. *J Am Coll Cardiol* 2013;**62**:D51–D59.
7. Coghlan JG, Denton CP, Grunig E, Bonderman D, Distler O, Khanna D, Muller-Ladner U et al.; DETECT study group. Evidence-based detection of pulmonary arterial hypertension in systemic sclerosis: the DETECT study. *Ann Rheum Dis* 2014;**73**:1340–1349.
8. Launay D, Sitbon O, Hachulla E, Mouthon L, Gressin V, Rottat L et al. Survival in systemic sclerosis-associated pulmonary arterial hypertension in the modern management era. *Ann Rheum Dis* 2013;**72**:1940–1946.
9. Sitges M, Shiota T, Lever HM, Qin JX, Bauer F, Drinko JK et al. Comparison of left ventricular diastolic function in obstructive hypertrophic cardiomyopathy in patients undergoing percutaneous septal alcohol ablation versus surgical myotomy/myectomy. *Am J Cardiol* 2003;**91**:817–821.